

SURGICAL RESEARCH EXPERIENCE

Section 1: Overview

The Department of Surgery encourages USUHS medical students to learn about surgical research. Interested students can see if they would like to make research a part of their medical career by participating in faculty research projects. Several faculty members are active in a variety of research fields. A list of faculty members and their research initiatives is summarized in Section 3. Interested students are encouraged to make inquiries by the contact mechanism provided in Section 3.

Section 2: Research Experiences Offered

The Department of Surgery offers four types of medical student research experiences.

- a. **MS IV Surgical Research Elective:** (4 or 8 weeks)
- b. **MS I Summer Research Experience:** This experience is made available to select medical students during the summer between their MSI and MSII years. Students with prior service who are exempt from the specific military training qualify for the research experience.
- c. **MS II Commandants Time:** Qualified students can spend a portion of their commandant's time participating in surgical research. Typically these students agree to interact with a particular research group over the entire academic year. Typically, a cumulative GPA of 3.0 or better and the Dean of the Students approval is needed to qualify for this experience.
- d. **Molecular Medicine Course:** A summer experience for qualified MS I and MS II students. Highly motivated students can participate in the Molecular Medicine Course taught by Dr. Elena Koustova. This comprehensive and intense course consists of daily lectures, experimental techniques sessions in the department molecular biology laboratory and analysis of pertinent medical literature. This course can serve to provide the core laboratory skills that can allow interested students to participate in scientific research throughout medical school.

NOTE

Each year students inquire about participating in research in order to gain co-authorship on a scientific publication to enhance their internship or residency application. We do not offer such a research experience and recommend students inquire with faculty at the clinical centers who may be able to support this type of request with case reports and small case series. The Department of Surgery faculty at USUHS primarily offers an educational and introductory experience in research. Often students do gain co-authorship, but this comes as a by-product of a major contribution, sustained over time and not a short-term primary goal.

Section 3: Faculty Members Participating in Research

- a. **Hasan Alam, MD**
All MS I-IV are welcome to work with the trauma research team. The research effort is funded by grants from the Office of Naval Research (ONR) and an R-01 grant from the National Institutes of Health. The ONR project has four areas of research; 1) hemorrhage control, 2) designing and testing of novel resuscitation fluids, 3) treatment of penetrating head injury and 4) development of new devices for battlefield application. The NIH project focuses on different aspects of induced hypothermic arrest in the treatment of traumatic shock. This research team consists of a practicing trauma surgeon, 2 PhDs, physicians, surgical residents and a number of support staff and lab technicians. Students interested in working with the trauma research team can inquire at halam@usuhs.mil

b. **William E. Bolger, MD, Chief, Division of Surgical Research.**

As an otolaryngologist, Dr. Bolger's primary research initiatives involve Sino nasal disease. Current research projects are exploring the basic pathophysiologic mechanisms in sinusitis. This research involves gene expression analysis of human Sino nasal polyposis biopsy specimens, small animal model studies of antigen presentation and the effect of viruses on host local Sino nasal immunity.

Dr. Bolger can currently provide a research experience for a small number of MS-IV students interested in dedicating 4 or preferably 8 weeks to a laboratory research project. For interested students, a more comprehensive experience is offered where by Dr. Bolger will mentor the students through the process of developing their own small research and submitting a small protocol through the USUHS – REA for funding. This experience would introduce the student to the process of writing a protocol /grant as well as conducting an experiment and writing a manuscript for publication. This experience would begin informally in MS III year. The research conducted during a research elective early in the MS IV year to allow time for the manuscript to be written during the winter and spring of the MS IV year prior to graduation. Interested students should inquire directly to Dr. Bolger at: wbolger@usuhs.mil

c. **Dr. Mark Bowyer, COL, MC, USAF**

Dr. Bowyer is a practicing trauma surgeon with many research Interests. As the Director of research at David Grant USAF Medical Center from 1991-1998, he was responsible for the oversight of multiple research fellows and numerous projects resulting in publication. Currently Dr. Bowyer is involved in ongoing trauma related research involving the use of blood substitutes as a bridge to definitive care, as well as exploration of novel approaches for delivering resuscitation, and preserving injured limbs.

As the current surgical director of the National Capital Area Medical Simulation Center, Dr. Bowyer is conducting ground breaking validation studies for incorporation of simulators into medical curriculum. His team at the Sim Center is also on the leading edge of developing new and improving old virtual reality simulators for the training of medical personnel. The Sim Cen is currently undergoing an exciting expansion with plans to build the worlds largest Computer Aided Virtual Environment or a CAVE (think of this as a first generation Star Trek holodeck). Prior to and upon completion of the CAVE there will be several exciting research challenges in developing and utilizing content in this project.

Students at all levels with an interest in either basic science/animal research, or an interest in the new frontier of simulation are encouraged to contact Dr. Bowyer for more information at: mbowyer@usuhs.mil

d. **Elena Koustova, Ph.D.**

The following is a brief description of some laboratory research activities that are performed during the Molecular Medicine Course. "We start with the familiarization with the central dogma of molecular biology: the biological information flows from DNA (gene) to RNA to protein, and the proteins determine our individual makeup or phenotype. During our first session we discuss the general structure of DNA and the ability of very special endonucleases, restriction enzymes, to recognize and cut double-stranded DNA at defined places (base sequences). In our lab experiment, we manipulate with large lambda phage DNA, which we cut using three different restriction enzymes. Since all three restriction enzymes digest DNA at different sites, digestion with each one of them produces a distinct pattern of DNA fragments of various lengths. The resulting DNA fragments are analyzed using agarose gel electrophoresis. Then we discuss two cases of serious outbreaks of surgical-site infections, one in California, and another in the Netherlands. Both hospitals had to suspend all elective surgery and request assistance in

investigation to determine and control the source of the outbreaks. In both cases, restriction analysis of clinical bacterial isolates was used to determine the potential source of bacteria. We discuss how specimens from the hospital environment and from staff hands were collected, digested with the enzymes and compared based on electrophoresis patterns.”

“Our second session deals with the DNA pieces - genes. We discuss the basic principles of genetics and talk specifically about the gene coding for tissue plasminogen activator gene (TPA). Using polymerase chain reaction (PCR) and our own cheek-cell DNA, we then look for the presence or absence of a small repetitive element called an Alu repeat (300 base-pair sequence) in the noncoding region of the tissue plasminogen activator (TPA) gene on chromosome 8. During evolutionary time, over 500,000 copies of the Alu repeat have been inserted, apparently at random, throughout the human genome. Within the eighth intron of the TPA gene, some people have an Alu insert and some do not. Following amplification, PCR products are analyzed using agarose gel electrophoresis and visualized using DNA gel stain. During the theoretical session we discuss the Rotterdam study (8000 subjects, 55 years and older), which showed that the presence of Alu insertion was associated with twice as many cases of myocardial infarction as was its absence.”

“Individual DNA molecules serve as templates for complementary RNA molecules during the process of transcription. Following the “central dogma” theory, our third session is dedicated to the RNA. We learn the RNA isolation, determination of RNA concentration and purity by UV spectroscopy, and RNA electrophoresis. We combine the technique of PCR that we learned previously with reverse transcription and master the most sensitive method of molecular biology – RT-PCR. Using RNA isolated from the animals subjected to the surgical procedures, we amplify and detect the expression of protective gene from the heat shock protein family – HSP 70. We learn that if we induce expression of HSP 70 before the surgical manipulations, the animal showing greater expression of HSP 70 (based on results of our RT-PCR experiment) is also showing the more favorable outcome after the surgery. We finish our experimental session by learning the method of high-resolution separation of small DNA fragments using vertical polyacrylamide electrophoresis. Very constructive theoretical discussion on whether the patient should be warmed before the elective surgery or not, then follows.”

“Next we concentrate our efforts on methods of protein analysis. Different ways of cell lysis with the help of various detergents and buffers are demonstrated. We learn how to make the cell release the intracellular proteins, how to collect them, determine their concentration and prepare the lysate for the Western blotting. The response of the brain tissue to traumatic brain injury is investigated by assessing the expression of two proteins – familiar HSP 70, which we study the day before on the gene level, and protein GFAP, which is heavily produced by the brain glial cells in response to any kind of insult.”

“We continue our journey into fascinating world of proteins by discussing their most unconventional function – participation in the process of the cell death. The mechanisms and different types of the cell death are illustrated using histochemistry and “in situ” apoptosis staining. “

“Our last session always proves to be the most exiting! We finally have a chance to see how by manipulating a single gene we can change (through the pathway we studied for two weeks: gene (DNA)-> RNA -> protein) the physical appearance or phenotype of the biological organism. In this lab, the students perform a procedure known as a genetic transformation. Transformation occurs when a cell takes up and expresses a new piece of genetic material (DNA). New piece of DNA can be cut out of human, animal, or plant DNA and placed inside different organism, like bacteria. This new genetic material often provides the organism with a new trait identifiable after

transformation. Genetic transformation literally means change caused by genes and it involves the insertion of a gene into an organism in order to change the organism's traits. We use a procedure to transform bacteria with the gene that codes for a Green Fluorescent Protein (GFP). The real-life source of GFP gene is the bioluminescent jellyfish *A. victoria*. The gene codes for a fluorescent protein, which causes the jellyfish to glow in the dark. We observe that following successful transformation procedure, our bacteria start to express their newly acquired jellyfish gene and produce the fluorescent protein, which caused them to glow a brilliant green color under the ultraviolet light. “

For interested students, please e-mail EKoustova@usuhs.mil

d. **David R. Welling, M.D., Associate Professor of Surgery.**

Dr. Welling is a colorectal surgeon and general surgeon, with main interests in clinical medicine. He would be interested in performing a clinically-relevant retrospective study involving the gastrointestinal tract with a student or small group of students. This study would be designed to fit the interests of the student(s). Possible topics to be explored might include such subjects as:

1. The patient with suspected appendicitis who undergoes an appendectomy which is “negative”. How often is that procedure done, and what other diagnoses are found to explain the patient's symptoms?
2. Long-term follow-up of active duty patients who have undergone ileoanal pouch surgery for ulcerative colitis or familial polyposis. What positions are they occupying within the military at present? Are they on any restrictions? Are they presently able to do their jobs fully?
3. The comparison between laparoscopic vs. open appendectomy. What is the rate of morbidity of the two operations? Can we recommend one over the other?

Interested students should inquire directly to Dr. Welling dwelling@usuhs.mil

f. **J. Leonel Villavicencio MD FACS. Professor of Surgery, USUHS**

Dr. Villavicencio is a cardiovascular surgeon, Director of the Venous and Lymphatic Surgical Clinic at WRAMC with experience in clinical and experimental research who offers students at any level, the opportunity to experience the challenge of clinical as well as experimental investigations in the field of venous diseases. Conception of a research project, search of the world literature, writing a protocol and time commitment to the realization of the study are discussed and implemented. The questions that need to be answered before embarking into a research project are: 1). **Why** did I select this topic? Does it have clinical application? Will it contribute to the understanding of a pathological process? 2). **How** am I going to do it ? resources, materials, patients, methodology, techniques, literature search etc. 3). **What** do I expect to obtain or clarify? What type of answers am I looking for? What type of results may I anticipate? (often this is a . very difficult question to answer since a planned experiment may change course in the middle due to unforeseen findings)

Students may become involved in any of the following protocols:

- A. At WRAMC. Using duplex ultrasound, and with the patient upright, determine the normal relationship between the caliber of the greater saphenous vein at the groin and mid-thigh and the body surface area in 25 normal individuals of both sex and in 25 patients with varicose veins of the lower extremities .Application?. Determine if a saphenous vein is normal or pathological in a given patient with symptoms of lower extremity discomfort, skin discoloration, leg cramps etc before varicose veins appear. This is useful in families with history of varicose veins who have teen- age daughters who will in the future experience the

venous overload of pregnancy. This is an example of research with direct clinical applications

- B. At USUHS, participating in any of the phases of going on research: human cadaver dissections to investigate the point of exit of the saphenous nerve from the fascia at distal medial thigh. Application? Prevent injury of the nerve and disabling saphenous neuritis during knee orthopedic operations, treatment of varicose veins by saphenous stripping, harvesting the saphenous vein for arterial by-pass or coronary surgery. Again, this is an example of research whose results are useful to the surgeons performing knee, venous or vascular and cardiac surgery. Anatomic knowledge is critically important!!
- C. At USUHS. Participating in the historical research of military medical education in other countries. How are military physicians educated in Germany, Poland, Russia, Austria, France, Mexico, USA, Japan, Italy, Spain etc. This is a fascinating search through the history of these countries and their efforts to educate military physicians for war and peace.
- D. If you are interested contact Dr Villavicencio at: lvillavicencio@usuhs.mil

g. **David Wherry, MD, Professor of Surgery.** 295-9834.

Each year we have a surgeon from the Philippine General Hospital and the University of the Philippines who spends a year doing research in our department. One of the current research projects is studying the molecular biology from tumor blocks of patients with colorectal cancer under the age of 40 years from the P.G.H. and comparing the findings to a matched group above age 40 years. In the United States about 5% of patients with colorectal cancer are under age 40 years, in contrast the patients under age 40 years from the Philippine General Hospital are 18% , the ? is why. At present the research scientist is a fully trained surgeon from PGH Dr. Russ Querol, we will be glad to discuss with any student who is interested their involvement in this ongoing research. For interested students please e-mail dwherry@usuhs.mil or rquerol@usuhs.mil

- h. **The Center for Prostate Disease Research** offers a variety of mechanisms for students to gain research exposure. Their main facility is located in Rockville which offers an outstanding basic science laboratory experience and an equally outstanding medical database research experience. Their clinical facility is located at Walter Reed as part of the urology service. CPDR also has a laboratory on site at USUHS which specialized in prostate cancer cell research.

Leon Sun, MD, PhD, Associate Professor of Surgery, Director of CPDR National Database.

CPDR National Database collects clinical information on patients with prostate cancer in nine military hospitals across the country. The database team composes of urologists, radiation oncologists, medical oncologists, nurses, clinical coordinators, programmers, developers, web masters and statisticians in addition to up to 1-3 well-trained data managers in the each hospitals. The main missions include collection and entry of clinical data, perform clinical research on the epidemiology, detection, diagnosis, treatment, control, prediction and prevention of prostate cancer. All MS I-IV are welcome to work with the database team. MS with research experience and MS IV are preferred. Students interested in working with the database team at CPDR's main headquarters in Rockville, M.D. can inquire at lsun@cpdr.org
Students interested in gaining research experience/exposure with CPDR at WRAMC can contact Stephanie.Shaar@NA.AMEDD.ARMY.MIL .